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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,052	06/02/2005	Allan Shepard	2335 US F	8397

7590 06/04/2010

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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
06/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,052	SHEPARD ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-8* is/are pending in the application.

4a) Of the above claim(s) *3-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*

DETAILED ACTION

Status of Application

1. The response filed February 4, 2010 has been received, entered and carefully considered. The response affects the instant application accordingly:

   a. Claim 1 has been amended.

2. Claims 1, 3-8 are pending in the case.

3. Claim 1 is present for examination.

4. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

5. All grounds not addressed in the action are withdrawn or moot.

6. New grounds of rejection are set forth in the current office action.

New Grounds of Rejection and Objection

The new grounds of rejection and objection are applied:

Objection of the Specification Under 37 C.F.R. §§ 1.821 - 1.825

7. The disclosure is objected to because of the following issues:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). See, for example, the primer sequence on page 20. However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825

because this sequence contains greater than or equal to ten amino acid molecules and does not have a SEQ ID NO. A thorough review and correction throughout the application is required.

Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicants are required to submit a new computer readable form sequence listing, a paper copy for the specification, statements under 37 CFR § 1.821(f) and (g), if there is a need to list additional sequences in the listing.

Applicants are given the same response time regarding this failure to comply as that set forth to respond to this Office Action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

Appropriate correction is required with statements that the CRF and paper copy are identical and statements that the CRF and paper copies do not add new matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claim recites the following terms: peptidomimetic aminomethyl ketones, α,α'-diacylamino ketones, alkoxymethyl ketones, α-alkoxylketones, cyanamides, N_{α}-acyl-α-amino acid-(arylaminoethyl)amides. There is inadequate written description for the terms to address the specific characteristics are for each term to be the defining relationship for the cathepsin K inhibition or a description for the degree of inhibition required to be viewed as a cathepsin K inhibitor. For example, the phrase peptidomimetic aminomethyl ketones does not recite a specific structure/function relationship as the phrase only requires the presence of an amino group, a ketone, and a methyl group wherein these elements are present in a multitude of forms (e.g. ring, linear, heterocycles, bulking groups, etc.) wherein the sterically all the compounds would not be able to have receptor interaction for cathepsin K inhibition (see Danziger et al.). Danziger et al. also acknowledges that there is a structure function relationship and that compounds that do not have the same structure (e.g. the various compounds per term, the various recited terms) are not likely to share the same function (i.e. lowering intraocular pressure). The same issues apply to the remaining terms above (i.e. alkoxymethyl ketones, , α,α'-diacylamino ketones, etc.). There is only a recitation of board classes of compounds with varying structure, activities and pharmacological profiles. There are also no representative examples. Therefore, the claimed invention is not supported by adequate written description.

9. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

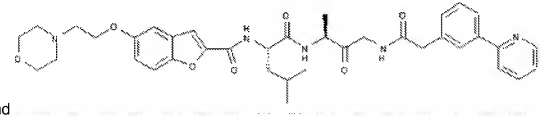
> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claim is directed to the use of a cathepsin K antagonist is selected from the group consisting of monensin, brefeldin A, 1,3-bis(acylamino)-2-propanone, cycloaltiliin 6, cycloaltiliin 7, 3-[2,4-dihydroxyphenyl]-propan-3-one (AC-3-1), 5,7,4'-trihydroxy-8-geranylflavanone (AC-3-3), 3,4,2',4'-tetrahydroxy-2-geranyldihydrochalcone (AC-5-1), haploscleridamine, 5-(2-morpholin-4-yl-ethoxy)-benzo furan-2-carboxylic acid ((S)-3-

methyl- 1-[3-oxo- 1-[2-(3-pyridin-2-yl-phenyl)-ethenoyl]-azepan-4-ylcarbanoyl]-butyl)-amide (SB-331750), N-[3-methyl- 1 (S)- [N- [3 -oxo- 1 -pyridin-2-ylsulfonyl)perhydroazepin-4(S)-yl] carbamoyl]butyl]- 1 - benzofuran-2-carboxamide (SB-357114), peptidomimetic aminomethyl ketones, α,α'-diacylamino ketones, alkoxymethyl ketones, α-alkoxylketones, cyanamides, N_{α}-acyl-α-amino acid-(arylaminoethyl)amides,



and

(SB-290190) for lowering intraocular pressure. The issues of written description for certain terms are addressed above.

Thus, the claims taken together with the specification imply that the administration of the cathepsin K inhibitors addressed above to a patient in need thereof (i.e. glaucoma) can decrease the ocular hypertension present, even though cathepsin K inhibition is neither known in the art be a relevant target for reducing pressure, nor substantiated/exhibited by Applicants' disclosure and there are no representative examples showing the reduction of pressure.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Woodward et al. (The inflow and outflow of anti-glaucoma drugs) teaches that drugs that lower intraocular pressure utilize typically one of two pathways-either reducing aqueous humor formation (inflow suppression) or improving the aqueous humor outflow (outflow enhancement). Some use both pathways (e.g. brimonidine). Examples of drugs that work by inflow suppression to lower intraocular pressure are

adrenergic agents such as B-adrenoceptor antagonists (e.g. timolol) and carbonic anhydrase inhibitors (e.g. acetazolamide). Drugs targeting outflow enhancement include pilocarpine (cholinergic), prostanoid FP receptor agonist (e.g. latanoprost, travoprost), and prostamides (e.g. bimatoprost).

Weinreb et al. teaches that the high intraocular pressure present in glaucoma is regulated by either suppressing aqueous inflow or increasing outflow (Page 1716). Common drugs include prostamides, carbonic anhydrase inhibitors, and alpha-2-adrenergic agonists; that can be administered in several ways including oral and topical.

As evidence by the art above in regards to the known modalities and difficulties for the reduction of intraocular pressure, the art is highly unpredictable.

There also in nothing present in the art to address cathepsin K inhibition to have any effect on either of these modalities of regulation of intraocular pressure.

(5) The relative skill of those in the art:

The skill of one in the art is high typically with medical and/or graduate education in the art, as one of skill in the art is well versed in ophthalmic therapies and in the understandings of the biological phenomena that relate to glaucoma and its associated symptoms. One of skill in the art either understands directly or is aware of the relevant art that teaches methods for monitoring intraocular pressure, the available known therapies for treating elevated pressure, the mechanisms of action and biological targets of the active, mechanisms of action in regards to the inflow and outflow pathways and fluctuations for addressing glaucoma, and the scientific methods for confirming these understandings (e.g., molecular biology and physiology for

ophthalmology). For example, compound X is know to work through receptor Y, the secondary effects of intraocular pressure, retinal neuropathy, and the associated receptors believed to be implicated.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification does not provide evidence or data showing a reduction in intraocular pressure in a patient with glaucoma. The specification does not show an association of the claimed cathepsin K inhibitors with the known conventional mechanisms for lowering intraocular pressure (i.e. inflow suppression or outflow enhancement of the aqueous humor) to indicate that the compounds are enabled to reduce the intraocular pressure. The art also does not indicate a mechanism for a reduction of intraocular pressure with the cathepsin K inhibitor.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the mechanism for reducing the intraocular pressure in a glaucoma patient and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims contains a number of lab designations (e.g. AC-5-1, AC-3-1), whereby the name is a lab designation which is analogous to tradenames and when used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A propriety lab name designation, trademark, or trade name is used to identify a source of goods, and not the goods themselves. Thus, a lab name designation, trademark, or trade name does not identify or describe the goods associated with the trademark or trade name.

Conclusion

11. Claim 1 is rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

/Frederick Krass/
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